

When rejecting a claim under 35 U.S.C. § 103, the Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). To establish a *prima facie* case the Examiner must show that the prior art reference, or references when combined, teach or suggest each and every limitation of the claimed invention. M.P.E.P. § 706.02(j). As discussed below, the Examiner has failed to establish that Guo *et al.* and Southern *et al.* teach or suggest each and every limitation of the claimed invention, and thus the Examiner has not established a *prima facie* case of obviousness in this case.

The two independent claims of the instant application, Claims 1 and 6, each comprise four steps: (1) hybridization of overlapping probes to a target nucleic acid; (2) determining the melting temperature of those probes and the target nucleic acid; (3) determining the difference between the melting temperature of the probes and the target and the melting temperature of the probes and a control nucleic acid (the difference is termed " $\Delta T_m$ "; (4) determining the difference between the  $\Delta T_m$  of two overlapping probes (termed the " $\Delta\Delta T_m$ ").

As pointed out by the Examiner, Guo *et al.* does not disclose the use of overlapping probes. Accordingly, Guo *et al.* cannot teach step (4) as described above. Southern *et al.* does not remedy this deficiency as Southern *et al.* does not teach or suggest determining the difference in  $\Delta T_m$  of two overlapping probes. Column 11, Lines 35-39 of Southern *et al.* (cited by the Examiner as teaching or suggesting step (4)) describes conditions where a perfectly matched probe/target pair will remain hybridized while probes having mismatches with the target will melt away. This teaching is significantly different from the instant invention. Comparing the differences between melting temperatures of various probes and a target can reveal the presence of sequence alterations, however such comparisons cannot reveal the location or identity of those sequence alterations. In contrast, the instant invention provides a method whereby both the location and identity of sequence alterations are revealed, by comparing the  $\Delta T_m$  for two overlapping probes. As neither Guo *et al.* or Southern *et al.* teach or suggest the comparison of  $\Delta T_m$  for two overlapping probes, the Examiner has not carried her burden in establishing a *prima facie* case of obviousness and the rejection under 35 U.S.C. 103(a) should be withdrawn

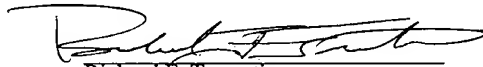
### CONCLUSION

On the basis of the remarks presented herein, Applicants believe that this application is now in condition for immediate allowance. Applicants respectfully request that the Examiner pass this application to issue, and early notice of such is requested. This paper is filed under 37 C.F.R. section 1.34(a).

Respectfully submitted,  
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